



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|------------------------|---------------------|-------------------------|
| 10/782,002 | 02/20/2004 | Arja Miettinen-Oinonen | 1716.051000A | 5790 |
| 26111 | 7590 | 10/24/2006 | | EXAMINER |
| STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005 | | | | PATTERSON, CHARLES L JR |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1652 | |

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---------------------------------------|--------------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/782,002 | MIETTINEN-OINONEN ET AL. | |
| | Examiner Charles L. Patterson, Jr. | Art Unit 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 14 August 2006.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 31-122 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) 31 and 33 is/are allowed.
 6) Claim(s) See Continuation Sheet is/are rejected.
 7) Claim(s) See Continuation Sheet is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 20 February 2004 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims rejected are 32,34,35,37,40,42,44-52,54,57,59,61-70,72,75,77,79-89,91,94,96,98-106,108,111,113 and 115-122.

Continuation of Disposition of Claims: Claims objected to are
36,38,39,41,43,53,55,56,58,60,71,73,74,76,78,90,92,93,95,97,107,109,110,112 and 114.

Art Unit: 1652

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 34-35, 37, 40, 42, 44-52, 54, 57, 59, 61-70, 72, 75, 77, 79-89, 91, 94, 96, 98-106, 108, 111, 113 and 115-122 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that (1) the amended claims are only directed to variants having cellulase activity and that the specification "provides a clear definition of equivalent amino acids... that do not essentially affect the biological activity of the protein..." and b) containing 'at least 80%-99% identity at the amino acid level'; (2) that "the issues raised by the Examiner are irrelevant to the question as to whether the claimed invention complies with the enablement requirement...[in that they] have already shown the claims are only directed to variants that have cellulase activity" (emphasis in original); (3) that the claims have now been amended to 90% identity; (4) that in the case of the 50K-cellulase B, 90% identity defines strict identity because this enzyme does not harbor the cellulase binding domain and its linker, unlike many other cellobiohydrolases, and 90% identity "would be nearly identical" to polypeptides having 100% identity; (5) "methods for making polypep-

Art Unit: 1652

tides that retain the biological activity of a known protein are known in the art" as shown in Bowie, et al. (V). Most fungal cellulases have a conserved domain consisting of a large catalytic domain and many have also a smaller cellulose binding domain separated by a distinct linker region and therefore given the teachings of the specification and information about cellulase conserved domains, one skilled in the art could easily make polypeptides having the cellulase activity in the instant claims.

The examiner does not agree and these points of argument are refuted with reference to the numbers *supra*.

(1) Although the specification makes these statements it does not disclose which specific amino acids can be substituted for which amino acids and still retain enzymatic activity. Applicants have amended the claims to 90% identity but the examiner has previously stated that he would allow 95% identity so as to take into account allelic variation. In this regard Guo, H.H., et al. (U) is cited. The reference teaches that "the overall probability of inactivating [the human DNA repair enzyme] with a single random amino acid change occurring randomly in the protein is" about 34% or 1/3 (last sentence of the paragraph spanning columns 1-2 on page 9206. Looking at the data from Table 1, the average mutation frequencies of 2.2, 4.6 and 6.2 amino acids are shown to have a % survival of $32.7 \pm 3.5\%$, $18.2 \pm 3.3\%$ and $10.7 \pm 2.3\%$. Since it is presuming that the DNA repair enzyme must be present in order for the organism to survive, this is an indication of the % survival of enzymatic activity. Taking .66 as the % of active mutants (the reciprocal of .34), then an approximate formula of $(.66)^x \times 100\%$ shows the percentage survival of "x" random mutations. Using this formula, the results for the data in Table 1 is 40, 15 and 8, which falls within the value actually found of $32.7 \pm 3.5\%$, $18.2 \pm 3.3\%$ and $10.7 \pm 2.3\%$. Therefore this formula shows a logarithmic relation-

Art Unit: 1652

ship and is a valid approximation of the amount of amino acid substitution that is allowed for an active enzyme. Of course this value could vary somewhat with different enzymes but should be valid as an approximation. In the present case, a mature protein of 452 amino acids (SEQ ID NO:35) are present and 90% identity would allow 45.2 amino acids changes. Using the formula above, this would calculate to $6.98 \times 10^{-7}\%$ active enzyme with 90% identity. 95% would calculate as $8.4 \times 10^{-3}\%$. Thus while 95% identity would require considerable experimentation to find active enzymes, it is deemed that 90% would require an inordinate amount of experimentation and with no guidance as to what specific amino acids to change and what to change them to, the claims should be limited to 95% identity.

(2) The issues raised are relevant to the enablement requirement in that the specification does not teach what specific residue can be changed to what and still retain enzymatic activity. It is maintained that undue experimentation would be required to practice the invention as claimed.

(3 & 4) As noted in the reply to (1) *supra*, 90% identity would require an inordinate amount of experimentation and even though the identity of the 50K-cellulose B would be higher than with the other enzymes claimed, it would still be an inordinate amount of experimentation.

(5) Although apparently most cellulases have a large catalytic domain and a smaller binding domain separated by distinct linker region, neither the teachings of Bowie, et al. (V) or Heikinheimo teach what specific residue can be changed to what in SEQ ID NO:35 and still have activity remain. As stated previously, the examiner will allow 95% identity.

Art Unit: 1652

Claims 31 and 33 are allowed. Claims 36, 38-39, 41, 43, 53, 55-56, 58, 60, 71, 73-74, 76, 78, 90, 92-93, 95, 97, 107, 109-110, 112 and 114 are objected to as being dependent upon a rejected base claim.

This action is being made non-final because the examiner omitted some claims from the 35 USC § 112 first paragraph rejection *supra* in the previous action. The other previous rejections under 35 USC § 112 first paragraph and the art rejections have been dropped in view of applicants' remarks.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the

Art Unit: 1652

Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
October 19, 2006